Diffusivity of Small Molecules in Fibrin and Poly (ethylene glycol) as Growth Plate Mimetic Carriers

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Introduction

The growth plate is a region of major importance in developing bone: it is the place where bone lengthening occurs by endochondral ossification. In order to recapitulate growth plate signaling in tissue engineered constructs, it is crucial that the mass transport characteristics of the carrier materials resemble those of the native growth plate. In this work, hydrogels made from fibrin and poly(ethylene glycol) (PEG) were evaluated as growth plate substitutes in terms of diffusion properties. These materials were selected for their differing architectures. Fibrin has an internal fibrous structure that can be altered by changing conditions of the enzyme-mediated polymerization during hydrogel formation. PEG hydrogels, on the other hand, form a mesh with porosity in the range of nanometers and do not exhibit any network structure at the microscale. Both hydrogel systems can be tuned to alter their chemical, biological and mechanical properties. Diffusion measurements were made using Fluorescence Recovery after Photobleaching (FRAP), a well-established method that is fast, precise and easy to use, with applications in a variety of situations[1].

Results

For fibrin hydrogels, it was found that changes in the network structure, achieved by varying the thrombin and factor XIII concentrations during polymerization, did not necessarily correspond to changes in diffusivity for small molecules in the range of the molecular weight of growth factors of interest (20 kDa). As expected, higher fibrinogen concentrations led to slower diffusion of dextran molecules; however, these differences were not dramatic, with values ranging from 58.4 to 64.6 $\mu m^2/s$ for fibrinogen concentrations of 20 to 5 mg/ml, respectively. On the contrary, PEG hydrogel density had a more substantial effect on the diffusion coefficient, with values ranging from 31.8 to 46.7 $\mu m^2/s$ for PEG concentrations of 150 to 25 mg/ml, respectively, and it appeared that the polymerization chemistry of the PEG hydrogel formation (acrylate or vinyl sulfone) also influenced the mass transport properties.

Conclusion

Fibrin and PEG hydrogels display tunable features that can be easily controlled to achieve desired mass transport properties and serve as growth plate mimetics. We have measured diffusion coefficients in the range of 32 to 65 $\mu m^2/s$, which is in line with measurement of the diffusion coefficients of molecules in the growth plate *in vitro*[2], which have been calculated to be between 10 and 70 $\mu m^2/s$.

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2. Williams, R. M., Zipfel, W. R., Tinsley, M. L. & Farnum, C. E. Solute transport in growth plate cartilage: in vitro and in vivo. *Biophysical journal* **93,** 1039–50 (2007).